REMARKS

Claim Rejections – 35 U.S.C. § 112

Claim 3 is rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite because it refers to Figure (1). Applicants respectfully traverse this basis for rejection.

According to MPEP § 2173.05(s):

> Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." *Ex parte Fressola*, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993) (citations omitted).

Consistent with MPEP § 2173.05(s), incorporation by reference of Figure (1) into claim 3 is necessary because it is more concise than duplicating the X-ray diffraction pattern into the claim. Further, incorporation by reference of X-ray diffraction patterns into patent claims is standard practice in the pharmaceutical compound art. *See, e.g.*, U.S. Patent Nos. 7,148,231, 7,074,928, 7,060,712, 7,015,238, 6,998,503, 6,958,337 and 6,900,221. In fact, the Primary Examiner on U.S. Patent No. 7,148,231 was James O. Wilson, who is Supervisory Examiner in this case. Accordingly, Applicants respectfully request reconsideration of this basis for rejection.

Claims 2 and 10 are rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite because they recite the relative term "substantially." According to the Examiner, the term "substantially" is not defined by the claim, the specification does not provide an appropriate standard, and one of ordinary skill in the art would not be

reasonably apprised of the scope of the invention. Applicants respectfully traverse this basis for rejection.

According to the MPEP 2173.05(b):

> The fact that claim language, including terms of degree, may not be precise, does not automatically render the claim indefinite under 35 U.S.C. 112, second paragraph. *Seattle Box Co., v. Industrial Crating & Packing, Inc.*, 731 F.2d 818, 221 USPQ 568 (Fed. Cir. 1984). Acceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification.

Applicants submit that, contrary to the Examiner's position, one skilled in the art would ascertain the scope of the claimed subject matter in light of the specification. The paragraph bridging pages 7 and 8 of the instant specification clearly delineates the scope of "substantially free of crystalline forms" recited in claims 2 and 10. Accordingly, Applicants respectfully request reconsideration of this basis for rejection.

Claim Rejections – 35 U.S.C. § 102

Claims 1-16 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Tang et al. (J. China Pharm. Univ., 2002; "Tang"), Pflum et al. (Organic Process Research & Development, 2001; "Pflum"), and Van de Venne et al. (U.S. patent 6,489,329; "Van de Venne"). According to the Examiner, Tang and Pflum teach the exact amorphous levocetirizine that falls within the range of Applicant's compounds. Van de Venne is said to teach compositions comprising levocetirizine dihydrochloride that falls within the range of Applicant's compounds with one or more pharmaceutically acceptable excipients. Applicants respectfully traverse this basis for rejection.

According to the MPEP § 2131:

> A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently descried, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 638, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Contrary to the Examiner's position, Tang does not disclose a compound having each and every limitation as set forth in claims 1-3 of the instant application. Claims 1-3 are directed to amorphous levocetirizine dihydrochloride. Although the English portions of Tang apparently disclose the isolation of levocetirizine dihydrochloride, there is no teaching or suggestion that the levocetirizine dihydrochloride is amorphous. Similarly, although Pflum discloses the synthesis of levocetirizine dihydrochloride, it does not teach or suggest that the levocetirizine dihydrochloride is amorphous.

With regard to Van de Venne, while Applicants agree that the reference discloses compositions comprising levocetirizine dihydrochloride with one or more pharmaceutically acceptable excipients, they are not the same compositions recited in claims 4-16. Claims 4-16 are directed to a pharmaceutical composition comprising amorphous levocetirizine dihydrochloride and one or more pharmaceutically acceptable excipients. As with Tang and Pflum, there is no teaching or suggestion that the levocetirizine dihydrochloride is amorphous. Applicants note that the Examiner apparently agrees with this conclusion, as the current Office Action at page 3 states that "Van de Venne teaches compositions comprising levocetirizine dihydrochloride," with the term "amorphous" conspicuously absent.

Applicants submit that it is error for the Examiner to ignore the element "amorphous." *See Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir.

1989) ("The identical invention must be shown in as complete detail as is contained in the . . . claim."). Because Tang, Plum and Van de Venne do not disclose amorphous levocetirizine dihydrochloride, claims 1-16 are not anticipated, and reconsideration of this basis for rejection is respectfully requested.

Claim Rejections – 35 U.S.C. § 103

Claims 17 and 18 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Van de Venne. According to the Examiner, Van de Venne teaches compositions comprising levocetirizine dihydrochloride. The Examiner acknowledges that the reference fails to disclose the claimed moisture content. However, according to the Examiner, it would have been obvious to one skilled in the art at the time of the invention to obtain the claimed composition because obviousness based on similarity of structure and function entails motivation to make the claimed compound in expectation that compounds similar in structure will have similar properties. In the case, according to the Examiner, the amorphous form is an obvious variation which one is motivated to obtain because of the expected solubility advantages (quoting from Hancock et al., *Pharm. Res.* 17:397-404 (2000)). Applicants respectfully traverse this basis for rejection.

According to MPEP § 706.02(j):

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on

> applicant's disclosure. *In re Vaeck,* 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Thus, to sustain the rejection of obviousness, the prior art reference must provide all the limitations of claims 17 and 18. Claims 17 and 18 are directed to a pharmaceutical composition comprising amorphous levocetirizine dihydrochloride and one or more pharmaceutically acceptable excipients and having a certain moisture content. As discussed above with respect to the § 102 rejection, Van de Venne fails to explicitly teach or suggest amorphous levocetirizine dihydrochloride, let alone the desirability of the claimed moisture content.

Applicants also submit that, contrary to the Examiner's assertion, the skilled artisan would not have been motivated to modify Van de Venne to obtain amorphous levocetirizine dihydrochloride for use in a pharmaceutical composition with a reasonable likelihood of success. Notwithstanding the fact that amorphous compounds tend to be more soluble than their crystalline counterparts, it remains the case that the pharmaceutical industry still faces significant challenges in the identification and isolation of amorphous pharmaceutical compounds. As explained by Almarsson & Gardner, *Curr. Drug Discov.* Jan., 21-26 (2003):

> Amorphous compounds carry inherent risks due to their physicochemical nature. In addition to being physically meta-stable (ie, prone to physical form changes such as crystallization), amorphous forms are generally less chemically stable in the solid state than the crystalline form. Amorphous compounds also tend to have very low bulk densities, making the materials difficult to isolate and handle. They also exhibit irregular particle properties and their high surface area often results in hygroscopicity (excessive moisture-sorption). These properties, despite presenting a potentially surmountable set of issues in discovery and early development, can cause major challenges in late-stage development. In general,

> pharmaceutical companies make every effort to avoid committing to the development of an amorphous compound. When sufficient quantities of such a compound become available, development scientists may obtain a crystalline form, the solubility of which can be dramatically (up to orders of magnitude) lower than that of the amorphous form. The decreased solubility frequently compromises or even abolishes oral absorption from the solid-state. This unsatisfying predicament leads to major resource expenditures in formulation development to recover *in vivo* performance. The resulting formulations often do not meet the criteria of chemical stability and processability, and hence the resulting dosage forms may limit the progress of a clinical program. As has already been stated, amorphous forms have, in rare cases, been chosen for development despite the risk of crystallization, an event that could cause a product to fail its critical performance criteria and regulatory specifications. The results of such an occurrence are disastrous for development programs, especially in late-stage trials where the formulation used is that intended for the market.

Based on the foregoing, Applicants submit that one of ordinary skill in the art could not predict with any certainty whether the amorphous form of a crystalline compound could be isolated without undue experimentation, even if such a motivation existed. Similarly, one of ordinary skill in the art could not predict with any certainty that the existence of a crystalline form of a compound necessarily indicates the existence of a stable amorphous form of the same compound.

Accordingly, claims 17 and 18 are not *prima facie* obvious over Van de Venne, and reconsideration of this basis for rejection is respectfully requested.

CONCLUSION

It is believed that claims 1-18 are now in condition for allowance, early notice of which would be appreciated. No fees are believed due at this time. If, however, any fees

are due, the Commissioner is authorized to charge any such fee to our Deposit Account No. 50-3221.

Respectfully submitted,

Dated: July 20, 2007

Milagros A. Cepeda
Attorney for Applicants
Reg. No. 33,365
Dr. Reddy's Laboratories, Inc.
200 Somerset Corporate Blvd.
Seventh Floor
Bridgewater, NJ 08807-2862
Tel. No.: 908-203-6505
Fax No.: 908-203-6515